REMARKS

Claims 1-23 are pending in the present application. Applicants acknowledge that claims 17, 18 and 20 are allowed. Claim 23 is canceled. Claim 1 is amended herein to specify that the nucleic acid including SEQ ID NO: 1 is an isolated sequence. Claims 2, 3 and 8 are also amended herein. Support for the amendments to claims 2 and 3 can be found in claims 2 and 3 as filed as well as in the specification, on page 3, lines 18-19. Support for the amendments to claim 8 can be found on page 3, lines 18-19 and on page 9, lines 23-24. Claim 6 is amended herein to correct the inadvertent omission of part of the accession number for plasmid pUC19PG. Support for this amendment can be found in claims 6 and 18 as filed. Claims 10-14, 16 and 22 are amended herein to correct a typographical error. These claims now recite "characterized" instead of "characterized." Claim 19 is also amended herein to correct a typographical error. Support for this amendment can be found in claims 7 and 19 as filed as well as in Figure 3. No new matter is believed to be added by these amendments. Therefore, pursuant to the following remarks, applicants respectfully request reconsideration of the application and allowance of the claims to issue.

Objections to the Drawings

The Office Action states that the drawings are objected to because Figure 7 contains text which recites the term "fig 2" and that this inconsistency requires correction.

In response, Applicants attach hereto a proposed corrected Figure 7 in which the superfluous text that was inadvertently included when filing the application is removed.

Thus, applicants believe this objection has been overcome and respectfully request its withdrawal.

Claim Objections

The Office Action states that claim 6 is objected to because the first three letters of the accession number are missing. The accession number should apparently read "DSM 12920."

The Examiner is correct in that the accession number should read "DSM 12920." Claim 6 is amended herein to recite "DSM 12920" with support in claims 6 and 18 as filed. Therefore, applicants believe this objection has been overcome and respectfully request its withdrawal.

Objection to the Specification

According to the Office Action, the disclosure is objected to because on page 5 of the specification, no dates of deposit have been provided. The Office Action also states that the address for the depository is wrong.

In response, Applicants have amended the specification to include the July 13, 1999 date of deposit. The specification has also been amended to recite "Braunschweig" instead of Brunswick. Therefore, Applicants believe this objection has been overcome and respectfully request its withdrawal.

Rejection Under 35 U.S.C. §101

The Office Action states that claim 1 is rejected under 35 U.S.C. § 101 because

the claimed invention is directed to non-statutory subject matter.

Claim 1 is amended herein to recite "an isolated nucleic acid including the nucleotide sequence of SEQ ID No 1." Therefore, Applicants believe the claim is now directed to statutory subject matter and respectfully request withdrawal of this rejection.

Rejection Under 35 U.S.C. § 102

The Office Action states that claims 2, 3, 8-11, 13, 14, 15, 16, 21 and 23 rejected under 35 U.S.C. 102(b) as being anticipated by Siekstele et al. (Yeast Vol. 15 no.4 1999). According to the Office Action, the invention of the instant claim is drawn to an expression vector comprising a nucleotide sequence of SEQ ID NO: 1, or a part thereof, a nucleotide sequence of SEQ ID NO:2, or a part thereof, and a nucleotide sequence of SEQ ID NO:3 and an insertion cloning site. The invention further comprises a foreign protein or peptide. The vector of the present claims is episomal and expressible in yeast. The invention further comprises a method for expressing a foreign protein or peptide by transforming a host cell with the claim expression vector.

Further stated in the Office Action is that Siekstele et al. disclose an episomal expression vector comprising a polynucleotide encoding the protein, EPG1 *of Kluyveromyces marxianus,* including a cloning site, terminator and an encoded signal sequence found between the promoter and the sequence encoding the EPG protein, plasmid pKEPEC. The construct also comprises a part of the promoter or SEQ ID NO: 1 including the TATA box, CAAT boxes and CT block (page 316, positions -513 to -1 of the figure depicted in figure 2, and Accession number A J000076). The construct comprises the signal sequence of SEQ ID NO:3 in addition to the terminator of SEQ ID

NO:2 in the construct pKEPEC (page 316, positions 1 to 75 and approximately positions 1146 to 1648 of figure 2, and Accession number AJ000076). Siekstele et al. further disclose--*K. marxianus* hosts with pKEPEC wherein the proteins encoded were expressed (page 318, column 2).

As stated above, claim 23 is canceled herein. As amended herein, claim 2 now recites "a yeast expression system containing in operative junction the nucleotide sequence of SEQ ID No 1, nucleotides 1-1134 of SEQ ID NO: 1 or a part of nucleotides 1-1134 of SEQ ID NO: 1 which is active as a promoter, an insertion cloning site and the nucleotide sequence of SEQ ID No 2 or a part thereof which is active as a terminator.

Similarly, claim 3 is amended herein to recite "a yeast expression and secretion system including in operative junction the nucleotide sequence of SEQ ID No 1, nucleotides 1-1134 of SEQ ID NO: 1 or a part of nucleotides 1-1134 of SEQ ID NO: 1 which is active as a promoter, the nucleotide sequence of SEQ ID No 3, an insertion cloning site and the nucleotide sequence of SEQ ID No 2 or a part thereof which is active as a terminator.

Also, claim 8 is amended herein to recite "an expression vector containing in operative junction a promoter with the sequence of SEQ ID No 1, the sequence of nucleotides 1-1134 of SEQ ID NO; 1 or a part of the sequence of nucleotides 1-1134 of SEQ ID NO: 1 which is active as a promoter, a polynucleotide which encodes a heterologous protein, and the nucleotide sequence of SEQ ID No 2 or a part thereof which is active as a terminator.

Applicants respectfully point out that Siekstele et al. does not disclose SEQ ID NO: 1, nucleotides 1-1134 of SEQ ID NO: 1 or a part of nucleotides 1-1134 of SEQ ID

NO: 1. The Examiner has stated that the only sequence provided by Siekstele et al. that functions as a promoter is nucleotides -513 to -1 of the nucleotide sequence depicted in Figure 2. Applicants point out that the promoter disclosed by Siekstele et al. is actually -571 to -1 of the nucleotide sequence depicted in Figure 2. Nucleotides -572 to -1 of the nucleotide sequence depicted in Figure 2 is not SEQ ID NO:1, nor is this sequence nucleotides 1-1134 of SEQ ID NO: 1, nor is this sequence a part of nucleotides 1-1134 of SEQ ID NO: 1. Therefore, Siekstele et al. does not disclose any of the promoter sequences recited in claims 2, 3 and 8. As amended herein, the yeast expression systems of claims 2, 3 and 8 contain SEQ ID NO: 1, nucleotides 1-1134 of SEQ ID NO:1 or a part of nucleotides 1-1134 of SEQ ID NO: 1 as a promoter. Thus, since Siekstele et al. does not disclose each and every element of the yeast expression system of claim 2, 3 or 8, this reference does not anticipate claims 2, 3, 8 or its dependent claims 9-11, 13-16 and 21.

Rejections Under 35 U.S.C. § 112, first paragraph

A. The Office Action states that claims 2, 3, 8-16, 21 and 22 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. The claim(s) allegedly contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Further stated in the Office Action is that the invention of the present claims is drawn to a nucleotide sequence of SEQ ID NO: 1 or a part thereof which is active as a promoter and a nucleotide sequence of SEQ ID NO:2 or a part thereof which is active as

a terminator. The present claims are allegedly drawn to undefined "parts," *i.e.* portions or fragments, of the claimed sequences having certain activities or function. In the case of SEQ ID NO: 1 the "parts" of the sequence have promoter activity; in the case of SEQ ID NO:2 the "parts" of the sequence have terminator activity. Thus, the Office concludes that the present claims are allegedly broad genus claims that encompass a wide array of molecules.

Further stated in the Office Action is that the specification does not disclose any of the parts, fragments or portions of either of SEQ ID NO: 1 or SEQ ID NO:2 embraced by the claims. Moreover, the Office Action asserts that the specification fails to disclose any teachings as to how the structures of these sequences relate to their function. Thus, according to the Office Action, the specification allegedly does not describe the complete structure of a representative number of species, partial structure and relevant identifying characteristics to adequately describe the present invention. Absent teachings and guidance as to the structure-function relationship of these molecules, the Office believes that specification allegedly does not describe the claimed sequence fragments in such full, clear, concise and exact terms so as to indicate to one of skill in the art that Applicant had possession of these molecules at the time of filing of the present application.

As amended herein, claims 2, 3 and 8 now recite, in relevant part, "the nucleotide sequence of SEQ ID No 1, nucleotides 1-1134 of SEQ ID NO: 1 or a part of nucleotides 1-1134 of SEQ ID NO: 1 which is active as a promoter." These claims also recite, in relevant part, " the nucleotide sequence of SEQ ID No 2 or a part thereof which is active as a terminator." Applicants have disclosed nucleotides 1-1134 of SEQ ID NO:1 as a

sequence which is active as a promoter. Applicants have also disclosed nucleotides 572-1134 of SEQ ID NO: 1 as a part of nucleotides 1-1134 of SEQ ID NO: 1 which is active as a promoter (page 10, lines 10-11 of the specification). Furthermore, it would be clear to one of skill in the art that upon disclosing nucleotides 1-1134 of SEQ ID NO: 1 and parts thereof, Applicants have also disclosed every subsesequence that is a part of nucleotides 1-1134 of SEQ ID NO: 1 and have therefore described the complete structure of each subsequence. For example, it would be clear to one of skill in the art that a part of nucleotides 1-1134 of SEQ ID NO:1 can be nucleotides 1-1133, nucleotides 1-1132, nucleotides 1-1131, nucleotides 2-1134, nucleotides 2-1133, nucleotides 2-1132 etc. because these subsequences are parts of a specifically defined nucleotide sequence. Thus, there is no question as to which nucleotides constitute a subsequence or a part of nucleotides 1-1134 of SEQ ID NO: 1. Furthermore, Applicants have provided a functional limitation for the claimed subsequences. It is clear that the present invention provides a function for nucleotides 1-1134 of SEQ ID NO: 1 as a promoter. Clear guidance for assessing promoter activity of the claimed subsequences or parts of nucleotides 1-1134 of SEQ ID NO: 1 is provided on pages 13-15 as well as throughout the specification where expression of heterologous proteins is described. Therefore, based on the teachings of the specification, it would be clear to one of skill in the art that Applicant was also in possession of subsequences or parts of nucleotides 1-1134 of SEQ ID NO: 1 that are active as a promoter.

Similarly, Applicants have disclosed SEQ ID NO 2 as a sequence which functions as a terminator. Applicants have also disclosed nucleotides 28-541 of SEQ ID NO: 2 as a part of nucleotides SEQ ID NO: 2 which functions as a terminator (page 10, lines 10-11

of the specification). Furthermore, it would be clear to one of skill in the art that upon disclosing nucleotides SEQ ID NO: 2 and parts thereof, Applicants have also disclosed every subsesequence that is a part of SEQ ID NO: 2 and have therefore described the complete structure of each subsequence. For example, it would be clear to one of skill in the art that a part of nucleotides SEQ ID NO: 2 can be nucleotides 1-541, nucleotides 1-540, nucleotides 539, nucleotides 2-541, nucleotides 2-540, nucleotides 2-539 etc. because these subsequences are parts of a specifically defined nucleotide sequence. Thus, there is no question as to which nucleotides constitute part of SEQ ID NO: 2. Furthermore, Applicants have provided a functional limitation for the claimed subsequences. It is clear that the present invention provides a function for SEQ ID NO: 2 as a terminator. Clear guidance for assessing terminator activity of the claimed subsequences or parts of nucleotides SEQ ID NO: 2 is provided on pages 13-15 as well as throughout the specification where expression of heterologous proteins is described. Therefore, based on the teachings of the specification, it would be clear to one of skill in the art that Applicant was also in possession of subsequences or parts of SEQ ID NO: 2 that function as a terminator.

B. The Office Action states that claims 2, 3, 8-16, 21 and 22 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the enablement requirement. According to the Office Action, the instant specification allegedly fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. An analysis of the *in re Wands* factors is also set forth in the Office Action.

According to Office Action, the specification allegedly does not disclose any of the "parts," fragments or portions of either of SEQ ID NO: 1 or SEQ ID NO: 2 embraced by the claims. Moreover, the specification allegedly fails to disclose any teachings as to how the structures of these sequences relate to their function. In other words, the Office concludes that the specification allegedly fails to disclose what sequence or domains of SEQ ID NO: 1 or SEQ ID NO:2 are required for a part, portion or fragment to maintain the claimed activities.

Applicants respectfully point out that in addition to SEQ ID NO: 1, the sequence of nucleotides 1-1134 of SEQ ID NO: 1 and the sequence of nucleotides 572 to 1134 are also disclosed as promoters. Similarly, in addition to SEQ ID NO: 2, applicants provide the sequence of nucleotides 28 to 541 of SEQ ID NO: 2 which functions as a terminator. Therefore, applicants do, in fact, provide portions of SEQ ID NO: 1 and SEQ ID NO: 2 that function as a promoter and terminator, respectively.

As set forth above, claims 2, 3 and 8 are amended herein to claim yeast expression systems which include parts of nucleotides 1-1134 of SEQ ID NO: 1 that are active as a promoter. Therefore, it would be routine for one of skill in the art to obtain a part of nucleotides 1-1134 of SEQ ID NO: 1 and assess its promoter activity. Based on well known techniques for assessing promoter activity and the teachings of the specification, it would be well within the abilities of a skilled artisan to determine which parts of nucleotides 1-1134 of SEQ ID NO: 1 are active as a promoter. Therefore, applicants believe sufficient guidance is provided in the instant specification for identification of parts of nucleotides 1-1134 of SEQ ID NO: 1 that are active as a promoter. Similarly, based on well known techniques and the teachings of the

specification, it would be routine for one of skill in the art to obtain a part of nucleotides SEQ ID NO: 2 and assess its terminator activity.

The Office Action further states that although the state of the art is high, it would be unpredictable to make parts or fragments of the presently claimed nucleic acid sequences which maintain their desired activity as a promoter (SEQ ID NO: 1) or terminator (SEQ ID NO:2). Further stated in the Office Action is that one of skill in the art may be able to screen for certain structural characteristics or function and that screening would not eliminate the unpredictability of false positive or negative results. For instance, according to the Office Action, one of skill in the art may make a construct comprising a part of the promoter of SEQ ID NO: 1, the promoter may have no activity or may have activity at such a basal level that the screens used by one of skill in the art would not be adequate to identify the construct.

As stated above, clear guidance for assessing the functional properties of a part of nucleotides 1-1134 of SEQ ID NO: 1 and a part of SEQ ID NO: 2 is provided on pages 13-15 and elsewhere throughout the specification where expression of heterologous proteins is described. Therefore, based on the teachings of the specification, one of skill in the art would know how to make and test any part of, nucleotides 1-1134 of SEQ ID NO: 1 to determine whether or not such a fragment retains biological activity, i.e. retains the ability to act as a promoter. Similarly, one of skill in the art would know how to make and test any part of SEQ ID NO: 2 to determine whether or not such a fragment retains biological activity, i.e. retains the ability to act as a terminator. Given the teachings of the specification, identifying functional fragments would require no more than routine experimentation.

In response to the Examiner's statement that one of skill in the art may make a construct comprising a part of the promoter of SEQ ID NO: 1 and the promoter may have no activity or may have activity at such a basal level that the screens used by one of skill in the art would not be adequate to identify the construct, Applicants respectfully point out that for enablement purposes, one of skill in the art need not know *a priori* what functions as a promoter, but need only be able to identify parts of nucleotides 1-1134 of SEQ ID NO; 1 that are active as a promoter The specification clearly sets forth the entire sequence of nucleotides 1-1134 of SEQ ID NO:1. Thus, it would be routine for one of skill in the art to obtain fragments of this sequence which can then be assayed to identify those sequences that are active as a promoter. Furthermore, assaying nucleotide sequences for promoter activity is considered routine in the art. Thus, even if the amount of experimentation may be large, because of its highly routine nature, the experimentation required would be considered to be routine. Thus, applicants believe that the claims are adequately enabled and respectfully request withdrawal of this rejection.

Rejections Under 35. U.S.C. § 112, second paragraph

The Office Action states that Claims 7, 19 and 23 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 7 and 19 refer to the same deposit accession number. However, the plasmid in claim 7 is recited as pEPG sec and the *E. coli in* claim 19 is recited as

pEPGseq. It is unclear whether the plasmid contained in the *E. coli* of claim 19 is the same as or different from the plasmid of claim 7 due to this inconsistency.

In response, claim 19 is amended herein to recite "pEPG sec" instead of pEPG seq". Thus, applicants believe this rejection has been overcome and respectfully request its withdrawal.

B. The Office Action states that claim 8 recites the phrase "foreign protein." This phrase is allegedly vague and indefinite because it is unclear whether Applicant intends the claim to mean a heterologous protein or any protein not found in the genome of the host cell.

Claim 8 is amended herein to recite "heterologous" instead of "foreign protein". Support for this amendment can be found in the specification on page 9, lines 23-24.

C. The Office Action states that claim 23 provides for the use of a DNA sequence according to SEQ ID NO: 1, but, since the claim does not set forth any steps involved in the method/process, it is allegedly unclear what method/process applicant is intending to encompass.

Claim 23 is canceled herein, thus rendering this rejection moot.

In view of the above amendments and remarks, reconsideration and allowance of the pending claims is believed to be warranted, and such action is respectfully requested. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issuance.

Enclosed is a Request for Extension of Time and Credit Card Form PTO-2038 authorizing payment in the amount of $950.00 to extend the period for reply by three months to September 24, 2004. It is believed that no additional fees are due. However, the Commissioner is hereby authorized to charge any deficiency or to credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date indicated below.

Lizette M. Fernandez — Date: 9/23/04